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09/703,753	11/01/2000	Robert E. Dudley	9774100-0024	2099

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EXAMINER
JIANG, SHAOJIA A

ART UNIT	PAPER NUMBER
1617	26

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/703,753	DUDLEY, ROBERT E.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *April 9, 2003 ,June 19, 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *211-214, 216-217, 219-223, 226-227, 229, 231, 234-252, 254, 359-361, 363-367, 369-370, and 372-376* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims pending in the application are 211-214,216,217,219-223,226,227,229,231,234 252,254,359-361,363-367,369,370 and 372-376.

DETAILED ACTION

Applicant's amendment and response filed April 9, 2003 in Paper No. 23 is acknowledged, wherein claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99, and 101-210 are cancelled, and claims 211-394 are newly submitted.

Applicant's Supplemental amendment and response filed on June 19, 2003 has been entered in Paper No. 25 wherein claims 215, 218, 224-225, 228, 230, 232-233, 253, 255-358, 362, 368, 371, and 377-394 are cancelled and claims 211-214, 216-217, 219-223, 226-227, 229, 231, 234-252, 254, 359-361, 363-367, 369-370, and 372-376 have been amended.

Currently, claims 211-214, 216-217, 219-223, 226-227, 229, 231, 234-252, 254, 359-361, 363-367, 369-370, and 372-376 are pending in this application.

Applicant's amendment canceling claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99, and 101-210, filed April 9, 2003 in Paper No. 23 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement in these claims of record stated in the Office Action dated January 15, 2003 has been fully considered and is found persuasive to remove the rejection since these claims have been cancelled. Therefore, the said rejection is withdrawn.

Applicant's amendment canceling claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99, and 101-210, filed April 9, 2003 in Paper No. 23 with respect to the rejection made under obviousness-type double patenting as being unpatentable

over claims 18-42 of U.S. Patent No. 6,503,894 of record stated in the Office Action dated January 15, 2003 has been fully considered and is found persuasive to remove the rejection since these claims have been cancelled. Therefore, the said rejection is withdrawn.

Applicant's amendment canceling claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99, and 101-210, filed April 9, 2003 in Paper No. 23 with respect to the rejection made under obviousness-type double patenting as being unpatentable over 1-21, 27, 53-55, 57-58, 60-64, and 79-145 of copending Application No. 10/033,101 of record stated in the Office Action dated January 15, 2003 has been fully considered and is found persuasive to remove the rejection since these claims have been cancelled. Therefore, the said rejection is withdrawn.

The following is new rejection(s) necessitated by Applicant's amendment filed April 9, 2003 in Paper No. 23 and Applicant's Supplemental amendment and response filed on June 19, 2003 in Paper No. 25, wherein all claims 33, 35-36, 41-42, 45, 48-49, 57-59, 62, 64, 75-83, 88-93, 97-99, and 101-210 rejected in the previous Office Action January 15, 2003 are cancelled.

Claim Objection

Claims 222 and 365 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The recitation "further comprises" ethanol and isopropyl alcohol (note that the term "alcohol" is missing in the claim) is employed in the dependent claims 222 and 365 is not further limit the subject matter of claims 211 and 359 since "a hydroalcoholic topical gel composition" has been recited in claims 211 and 359.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 234 and 240-248 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for co-administering testosterone and the particular other agent or pharmaceutical disclosed in the specification (see page 47-50 of the specification herein) in methods herein, does not reasonably provide enablement for improving the efficacy of any pharmaceuticals useful for treating erectile dysfunction in a male, for the same reasons of record stated in the Office Action dated January 15, 2003, the rejection made under 35 U.S.C. 112, first paragraph for lack of scope of enablement for the same recitation "pharmaceutical".

As discussed in the previous Office Action, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of any pharmaceuticals having the function of treating erectile dysfunction recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of

any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, and *In re Fisher* (CCPA 1970) discussed in the previous Office Action, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 241 and 366 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to the employment of a combination of active agents "has a synergistic effect in treating erectile dysfunction".

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to methods of treating erectile dysfunction, or treating sexual dysfunction.

The relative skill of those in the art: The relative skill of those in the art is high.

In regard to the following *Wands* factors, the predictability or unpredictability of the art; the amount of direction or guidance presented; the presence or absence of working examples as discussed below:

The instant claimed invention is highly *unpredictable*. Synergistic or superadditive effects for combinations of compounds are highly unpredictable. In the instant case there is insufficient guidance and **no** working examples in the specification showing that

the particular agents in specific amounts to be combined achieved synergistic effects in the method of treating erectile dysfunction, or treating sexual dysfunction herein. It is noted that the specification merely states that "Applicant expects that all test parameters will show improvement and synergy with the combination" (see page 54 lines 15-16 of the specification herein, emphasis added). Thus, the specification fails to demonstrate any synergistic effects produced by the combination herein.

Therefore, in view of the *Wands* factors discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims whether they produced a synergistic effect in treating erectile dysfunction, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 234 and 240-248 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "more effective" in claim 234 is a relative term which renders claims 234 and 240-248 indefinite. The term "more" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 211-214, 216-217, 219-223, 226-227, 229, 231, 234-252, 254, 359-361, 363-367, 369-370, and 372-376 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omar (5,730,987, of record) and Mak et al. (WO 99/24041, of record) and Moreland et al.(of recohrd) in view of Allen (WO 96/227372, of record) and Heiber et al. (WO 93/25168, of record).

Omar discloses that the particular steroid, testosterone and yohimbine or papaverin in a combination to be administered are useful in the composition and the method of the treatment of impotent in human males, i.e., erectile dysfunction. See col.1 lines 17-65 and claims 6-8.

Mak et al. discloses an enhancement of the penetration of transdermally (percutaneously) or topically applied a pharmaceutical composition comprising an active agent, testosterone, and a penetration-enhancing system that comprises oleic acid (a fatty acid having 17 carbon atoms), C1-C4 alcohol (e.g., ethanol, 2-propanol), and the gelling agent (a thickener), CARBOPOL (a polyacrylic acid). See abstract, page 3 lines 1-5, page 10 Example 1, and Figure 2.

Heiber et al. (WO 93/25168) discloses that testosterone compositions comprising a transdermal (percutaneous) delivery system comprising C2 or C3 alcohol, a penetration enhancer therein, i.e., glycerine, and a gelling agent, are useful in methods moderating and maintaining transdermal drug delivery to the derma at a relatively sustained rate over the duration of application to situs. See abstract, Example 3 at page 19-21, and claims 1-46 and 48.

The prior art does not expressly disclose a method of treating erectile dysfunction in a male comprising the particular composition comprising testosterone, C1-C4 alcohol, and the particular penetration enhancer, isopropyl myristate, and the effective amounts of active ingredients in combination with another pharmaceutical useful for treating the same erectile dysfunction such as sildenafil.

Moreland et al. teaches that the phosphodiesterase type 5 inhibitor, sildenafil, is useful in the treatment of male erectile dysfunction. See Abstract and Introduction.

Allen discloses a topical cream composition useful for treating male erectile dysfunction comprising the particular penetration enhancer, isopropyl myristate or glycerine. See abstract and claim 1 and 4.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular composition comprising testosterone, C1-C4 alcohol, and the particular penetration enhancer, C8-C22 fatty acid and isopropyl myristate, and in combination with another pharmaceutical useful for treating erectile dysfunction such as sildenafil in methods for treating the same.

One having ordinary skill in the art would have been motivated to employ the particular steroid, testosterone, C1-C4 alcohol, and the particular penetration enhancer, C8-C22 fatty acid and isopropyl myristate in a method for improving the efficacy of the composition herein useful for treating erectile dysfunction in an eugonadal male since the composition containing testosterone of Mak et al. is known to be useful in a method for improving the efficacy of percutaneously delivering a pharmaceutical because this composition further comprises a transdermally or topically penetration-enhancing system encompassing an oleic acid (a fatty acid having 17 carbon atoms), C1-C4 alcohol (e.g., ethanol, 2-propanol), and a penetration enhancer and a gelling agent. Moreover, the teachings of Heiber et al. have further provided the motivation to make the present invention since testosterone compositions of Heiber are known to comprise a transdermal (percutaneous) delivery system comprising C2 or C3 alcohol, a penetration enhancer therein, i.e., glycerine, and a gelling agent, and these compositions are known to be useful in methods moderating and maintaining transdermal drug delivery to the derma at a relatively sustained rate over the duration of application to situs.

Therefore, one of ordinary skill in the art would have found it obvious to employ the composition of Mak et al. in the instant claimed method. The topical cream composition of Allen is also known to be useful for treating male erectile dysfunction comprising the particular penetration enhancer herein, isopropyl myristate, which provides additional motivation for the claimed method. Thus, the motivation to employ known drug delivery systems to enhance the penetration of actives herein transdermally

(percutaneously) or topically for treating male erectile dysfunction is clearly provided by the Mak et al. and Allen references.

Further, the particular steroid, testosterone, is well known to be useful to treat erectile dysfunction in a male according to Omar. Moreover, all another pharmaceutical employed in the combination with testosterone recited in claims, i.e., claim 211 (b), are well known in the art to be useful in treating erectile dysfunction in a male.

Therefore, one of ordinary skill in the art would have reasonably expected that adding another pharmaceutical useful for treating erectile dysfunction such as sildenafil sildenafil to Mak's composition would improve the therapeutic effect of Mak's composition to treat male erectile dysfunction.

It has been held that it is prima facie obvious to combine two agents each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06. Furthermore, the motivation for the combination herein has been provided by the teachings of Omar.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active ingredients in the composition because the optimization of known effective amounts of known active agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill

in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

As discussed above, the record contains no clear and convincing evidence of nonobviousness or unexpected results for the combination method herein over the prior art. In this regard, it is noted that the specification provides no side-by-side comparison with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a).

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
August 22, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

8/25/03